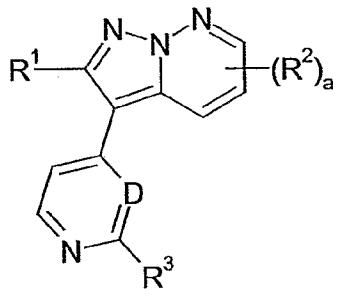
CLAIMS

We claim:

1. A compound of Formula (I):



(I)

or a salt, solvate, or physiologically functional derivative thereof:

wherein:

D is N or CH

R^1 is hydrogen, C_1-C_6 alkyl, C_2-C_4 alkenyl, C_2-C_4 alkynyl, C_1-C_3 alkoxy, halogen, $-CF_3$, hydroxy, cyano, $-S(O)_yC_1$-C_3 alkyl, or $-NR^4R^5$;

y is 0, 1, or 2;

a is 1 or 2;

R^2 is hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 haloalkyl, C_3-C_7 cycloalkyl, halogen, heterocyclyl, aryl, heteroaryl, cyano, azido, nitro, $-OR^8$, $-OR^6R^8$, $-R^6R^7$, $-R^6R''$, $-OS(O)_2R^9$, $-S(O)_yR^{10}$, $-C(O)R^7$, $-C(O)OR^7$, $-C(O)NR^4R^5$, $-N(H)R'C(=NR^4)NR^4R^5$, $-OC(O)NR^4R^5$, $-OC(O)OR^7$, $-C(=NR^4)NR^4R^5$, $-NR^4R^5$, $-OC(O)R^7$, or $-N(R^8)C(O)R^8$;

R^3 is $-(Q)_p-(Q^1)$

where

Q is O, $N(R^8)$ or $S(O)_y$, p is 0 or 1, y is 0, 1, or 2 and

Q^1 is C_1-C_6 alkyl, C_3-C_7 cycloalkyl, C_1-C_6 haloalkyl, aryl, aryl substituted with $-C(O)N(H)R^6NR^4R^5$ or $-OC(H)(OH)R^6NR^4R^5$, heteroaryl, aralkyl, or $-R^6NR^4R^5$;

R^4 and R^5 are independently hydrogen, C_1-C_3 alkyl, C_3-C_7 cycloalkyl, $-C(O)R^9$, or R^4 and R^5, together with the nitrogen atom to which they are bound, form a heterocyclyl;

R^6 is alkylene, arylene, heteroarylene, C_3-C_7 cycloalkylene, alkenylene, C_3-C_7 cycloalkenylene, or alkynylene;

R^7 is hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, $-NR^4R^5$, aryl, aralkyl, heteroaryl, cycloalkyl, heterocyclyl, $-S(O)_yR^{10}$, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^4R^5$, $-S(O)_2NR^4R^5$, $-N(H)R'C(=NR^4)NR^4R^5$, $-OC(O)NR^4R^5$, $-OC(O)OR^8$, $-C(=NR^4)NR^4R^5$, $-NR^4R^5$, or $-N(R^8)C(O)R^8$;

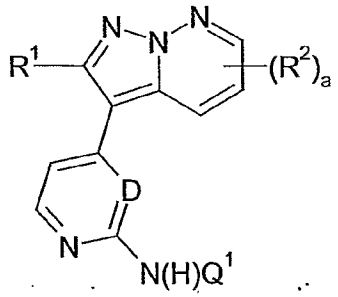
R^8 is hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, $-NR^4R^5$, aryl, aralkyl, heteroaryl, cycloalkyl, heterocyclyl, or $-S(O)_2R^9$;

R^9 is C_1-C_6 alkyl or C_1-C_6 haloalkyl;

R^{10} is hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, $-NR^4R^5$, aryl, aralkyl, heteroaryl, cycloalkyl, heterocyclyl, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^4R^5$, $-N(H)R'C(=NR^4)NR^4R^5$, $-OC(O)NR^4R^5$, $-OC(O)OR^8$, $-C(=NR^4)NR^4R^5$, $-NR^4R^5$, or $-N(R^8)C(O)R^8$;

R' is C_1-C_3 alkylene; and
R'' is $-OR^7$, $-OC(O)NR^4R^5$, $-OC(O)OR^7$, or $-OC(O)R^7$.

2. A compound of Formula (II):



(II)

or a salt, solvate, or physiologically functional derivative thereof:
wherein:

D is N or CH;

R^1 is hydrogen, C_1-C_6 alkyl, C_2-C_4 alkenyl, C_2-C_4 alkynyl, C_1-C_3 alkoxy, $-CF_3$, halogen, hydroxy, cyano, $-S(O)_yC_1$-C_3 alkyl, or $-NR^4R^5$;

y is 0, 1, or 2;

a is 1 or 2;

R^2 is hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 haloalkyl, C_3-C_7 cycloalkyl, halogen, heterocyclyl, aryl, heteroaryl, cyano, azido, nitro, $-OR^8$, $-OR^6R^8$, $-R^6R^7$, $-R^6R''$, $-OS(O)_2R^9$, $-S(O)_yR^{10}$, $-C(O)R^7$, $-C(O)OR^7$, $-C(O)NR^4R^5$, $-N(H)R'C(=NR^4)NR^4R^5$, $-OC(O)NR^4R^5$, $-OC(O)OR^7$, $-C(=NR^4)NR^4R^5$, $-NR^4R^5$, $-OC(O)R^7$, or $-N(R^7)C(O)R^7$;

Q^1 is C_1-C_6 alkyl, C_3-C_7 cycloalkyl, C_1-C_6 haloalkyl, aryl, aryl substituted with $-C(O)N(H)R^6NR^4R^5$ or $-OC(H)(OH)R^6NR^4R^5$, heteroaryl, aralkyl, or $-R^6NR^4R^5$;

R^4 and R^5 are independently hydrogen, C_1-C_3 alkyl, C_3-C_7 cycloalkyl, $-C(O)R^9$, or R^4 and R^5, together with the nitrogen atom to which they are bound, form a heterocyclyl;

R^6 is alkylene, arylene, heteroarylene, C_3-C_7 cycloalkylene, alkenylene, C_3-C_7 cycloalkenylene, or alkynylene;

R^7 is hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, $-NR^4R^5$, aryl, aralkyl, heteroaryl, cycloalkyl, heterocyclyl, $-S(O)_yR^{10}$, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^4R^5$, $-S(O)_2NR^4R^5$, $-N(H)R'C(=NR^4)NR^4R^5$, $-OC(O)NR^4R^5$, $-OC(O)OR^8$, $-C(=NR^4)NR^4R^5$, $-NR^4R^5$, or $-N(R^7)C(O)R^7$;

R^8 is hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, $-NR^4R^5$, aryl, aralkyl, heteroaryl, cycloalkyl, heterocyclyl, or $-S(O)_2R^9$;

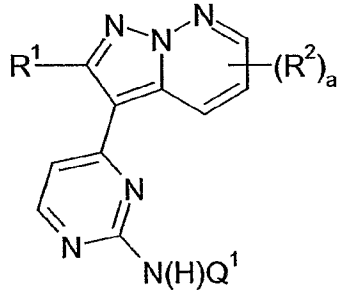
R^9 is C_1-C_6 alkyl or C_1-C_6 haloalkyl;

R^{10} is hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, $-NR^4R^5$, aryl, aralkyl, heteroaryl, cycloalkyl, heterocyclyl, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^4R^5$, $-N(H)R'C(=NR^4)NR^4R^5$, $-OC(O)NR^4R^5$, $-OC(O)OR^8$, $-C(=NR^4)NR^4R^5$, $-NR^4R^5$, or $-N(R^8)C(O)R^8$;

R' is C_1-C_3 alkylene; and

R'' is $-OR^7$, $-OC(O)NR^4R^5$, $-OC(O)OR^7$, or $-OC(O)R^7$.

3. A compound of Formula (III):



(III)

or a salt, solvate, or physiologically functional derivative thereof:

wherein:

R^1 is hydrogen, C_1-C_6 alkyl, C_2-C_4 alkenyl, C_2-C_4 alkynyl, C_1-C_3 alkoxy, $-CF_3$, halogen, hydroxy, cyano, $-S(O)_yC_1$-C_3 alkyl, or $-NR^4R^5$;

y is 0, 1, or 2;

a is 1 or 2;

R^2 is hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 haloalkyl, $-CF_3$, C_3-C_7 cycloalkyl, halogen, heterocyclyl, aryl, heteroaryl, cyano, azido, nitro, $-OR^8$, $-OR^6R^8$, $-R^6R^7$, $-R^6R''$, $-OS(O)_2R^9$, $-S(O)_yR^{10}$, $-C(O)R^7$, $-C(O)OR^7$, $-C(O)NR^4R^5$, $-N(H)R'C(=NR^4)NR^4R^5$, $-OC(O)NR^4R^5$, $-OC(O)OR^7$, $-C(=NR^4)NR^4R^5$, $-NR^4R^5$, $-OC(O)R^7$, or $-N(R^7)C(O)R^7$;

Q^1 is C_1-C_6 alkyl, C_3-C_7 cycloalkyl, C_1-C_6 haloalkyl, aryl, aryl substituted with $-C(O)N(H)R^6NR^4R^5$ or $-OC(H)(OH)R^6NR^4R^5$, heteroaryl, aralkyl, or $-R^6NR^4R^5$;

R^4 and R^5 are independently hydrogen, C_1-C_3 alkyl, C_3-C_7 cycloalkyl, $-C(O)R^9$, or R^4 and R^5, together with the nitrogen atom to which they are bound, form a heterocyclyl;

R^6 is alkylene, arylene, heteroarylene, C_3-C_7 cycloalkylene, alkenylene, C_3-C_7 cycloalkenylene, or alkynylene;

R^7 is hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, $-NR^4R^5$, aryl, aralkyl, heteroaryl, cycloalkyl, heterocyclyl, $-S(O)_yR^{10}$, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^4R^5$, $-S(O)_2NR^4R^5$, $-N(H)R'C(=NR^4)NR^4R^5$, $-OC(O)NR^4R^5$, $-OC(O)OR^8$, $-C(=NR^4)NR^4R^5$, $-NR^4R^5$, or $-N(R^7)C(O)R^7$;

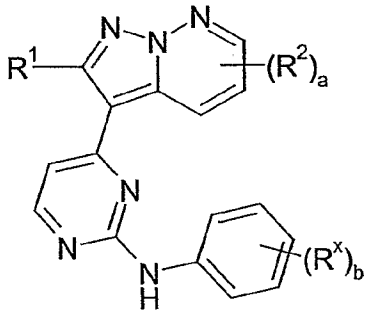
R^8 is hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, $-NR^4R^5$, aryl, aralkyl, heteroaryl, cycloalkyl, heterocyclyl, or $-S(O)_2R^9$;

R^9 is C_1-C_6 alkyl or C_1-C_6 haloalkyl;

R^{10} is hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, $-NR^4R^5$, aryl, aralkyl, heteroaryl, cycloalkyl, heterocyclyl, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^4R^5$, $-N(H)R'C(=NR^4)NR^4R^5$, $-OC(O)NR^4R^5$, $-OC(O)OR^8$, $-C(=NR^4)NR^4R^5$, $-NR^4R^5$, or $-N(R^8)C(O)R^8$;

R' is C_1-C_3 alkylene; and
R'' is $-OR^7$, $-OC(O)NR^4R^5$, $-OC(O)OR^7$, or $-OC(O)R^7$.

4. A compound of Formula (IV):



(IV)

or a salt, solvate, or physiologically functional derivative thereof:
wherein:

R^1 is hydrogen, C_1-C_6 alkyl, C_2-C_4 alkenyl, C_2-C_4 alkynyl, C_1-C_3 alkoxy, C_1-C_6 haloalkyl, halogen, hydroxy, cyano, $-S(O)_yC_1$-C_3 alkyl, or $-NR^4R^5$;

y is 0, 1, or 2;

a is 1 or 2;

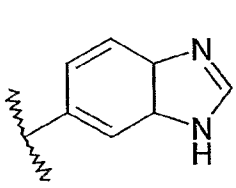
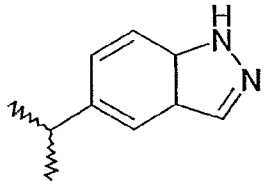
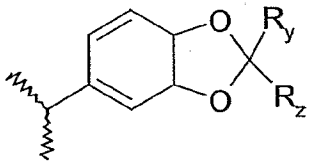
R^2 is hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 haloalkyl, C_3-C_7 cycloalkyl, halogen, heterocyclyl, aryl, heteroaryl, cyano, azido, nitro, $-OR^8$, $-OR^6R^8$, $-R^6R^7$, $-R^6R''$, $-OS(O)_2R^9$, $-S(O)_yR^{10}$, $-C(O)R^7$, $-C(O)OR^7$, $-C(O)NR^4R^5$, $-N(H)R'C(=NR^4)NR^4R^5$, $-OC(O)NR^4R^5$, $-OC(O)OR^7$, $-C(=NR^4)NR^4R^5$, $-NR^4R^5$, $-OC(O)R^7$, or $-N(R^7)C(O)R^7$;

b is 1, 2, or 3;

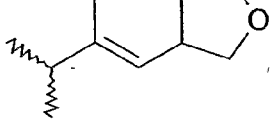
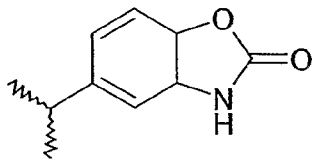
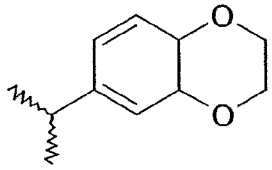
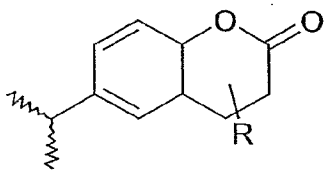
R^x is independently selected from hydrogen, halogen, C_1-C_6 alkyl, C_1-C_6 hydroxyalkyl, -CN, $-C(O)OH$, $-OC(O)R^{11}$, C_1-C_6 haloalkyl, $-NO_2$, -OH, $-OR^9$, aryl, heteroaryl, heterocyclyl, $-NR^4R^5$, $-R^6NR^4R^5$, $-C(O)N(H)R^6NR^4R^5$, $-S(O)_yR^{10}$, $-SO_2OH$,

or

b is 2 and the two R^x groups together with the phenyl group to which they are bound form a fused group selected from:


,

,

,

wherein R_y and R_z are independently selected from hydrogen and halogen,


,

,

,


, wherein R is selected from –CF3, halogen, or hydrogen;

R^4 and R^5 are independently hydrogen, C_1-C_3 alkyl, C_3-C_7 cycloalkyl, $-C(O)R^9$, or R^4 and R^5, together with the nitrogen atom to which they are bound, form a heterocyclyl;

R^6 is alkylene, arylene, heteroarylene, C_3-C_7 cycloalkylene, alkenylene, C_3-C_7 cycloalkenylene, or alkynylene;

R^7 is hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, $-NR^4R^5$, aryl, aralkyl, heteroaryl, cycloalkyl, heterocyclyl, $-S(O)_yR^{10}$, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^4R^5$, $-S(O)_2NR^4R^5$, $-N(H)R'C(=NR^4)NR^4R^5$, $-OC(O)NR^4R^5$, $-OC(O)OR^8$, $-C(=NR^4)NR^4R^5$, $-NR^4R^5$, or $-N(R^7)C(O)R^7$;

R^8 is hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, $-NR^4R^5$, aryl, aralkyl, heteroaryl, cycloalkyl, heterocyclyl, or $-S(O)_2R^9$;

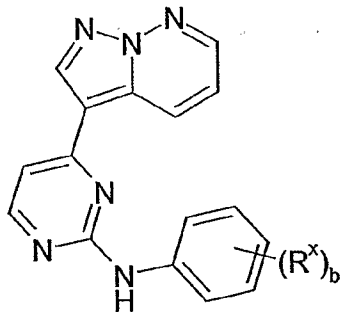
R^9 is C_1-C_6 alkyl or C_1-C_6 haloalkyl;

R^{10} is hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, $-NR^4R^5$, aryl, aralkyl, heteroaryl, cycloalkyl, heterocyclyl, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)NR^4R^5$, $-N(H)R'C(=NR^4)NR^4R^5$, $-OC(O)NR^4R^5$, $-OC(O)OR^8$, $-C(=NR^4)NR^4R^5$, $-NR^4R^5$, or $-N(R^8)C(O)R^8$;

R^{11} is C_1-C_6 alkyl;

R' is C_1-C_3 alkylene; and
R'' is $-OR^7$, $-OC(O)NR^4R^5$, $-OC(O)OR^7$, or $-OC(O)R^7$.

5. A compound of Formula (IVa):



(IVa)

or a salt, solvate, or physiologically functional derivative thereof:

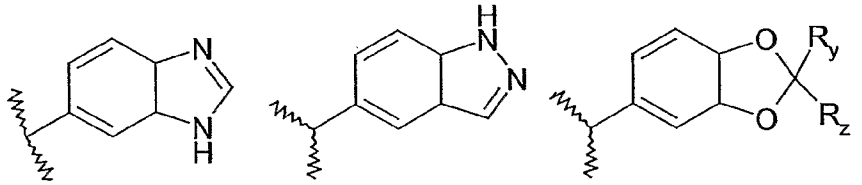
b is 1, 2, or 3;

y is 0, 1, or 2;

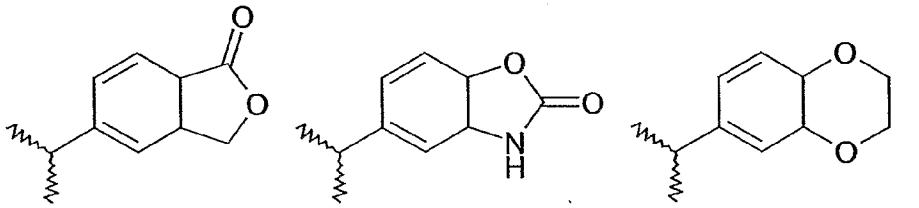
R^x is independently selected from hydrogen, halogen, C_1-C_6 alkyl, C_1-C_6 hydroxyalkyl, -CN, -C(O)OH, -OC(O)R^{11}, C_1-C_6 haloalkyl, -NO_2, -OH, -OR^9, aryl, heteroaryl, heterocyclyl, -NR^4R^5, -$R^6NR^4R^5$, -C(O)N(H)$R^6NR^4R^5$, -$S(O)_yR^{10}$, -SO_2OH,

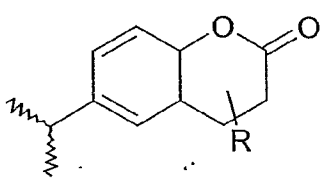
or

b is 2 and the two R^x groups together with the phenyl group to which they are bound form a fused group selected from:



wherein Ry and Rz are independently selected from hydrogen and halogen,





, wherein R is selected from -CF3, halogen, or hydrogen;

R^4 and R^5 are independently hydrogen, C_1-C_3 alkyl, C_3-C_7 cycloalkyl, $-C(O)R^9$, or R^4 and R^5, together with the nitrogen atom to which they are bound, form a heterocyclyl;

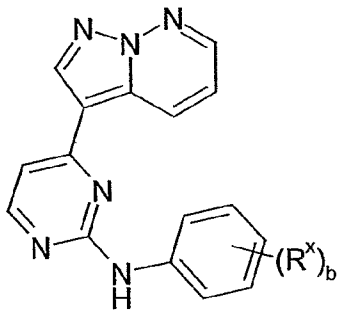
R^6 is alkylene, arylene, heteroarylene, C_3-C_7 cycloalkylene, alkenylene, C_3-C_7 cycloalkenylene, or alkynylene;

R^9 is C_1-C_6 alkyl or C_1-C_6 haloalkyl;

R^{10} is NH_2, C_1-C_6 alkyl, C_1-C_6 hydroxyalkyl, aryl, heteroaryl, or heterocyclyl; and

R^{11} is C_1-C_6 alkyl.

6. A compound of Formula (IVa):



(IVa)

or a salt, solvate, or physiologically functional derivative thereof:

b is 1, 2, or 3;

y is 0, 1, or 2;

R^x is independently selected from hydrogen, halogen, C_1-C_6 alkyl, C_1-C_6 hydroxyalkyl, -CN, $-C(O)OH$, $-OC(O)R^{11}$, C_1-C_6 haloalkyl, $-NO_2$, -OH, $-OR^9$, aryl, heteroaryl, heterocyclyl, $-NR^4R^5$, $-R^6NR^4R^5$, $-C(O)N(H)R^6NR^4R^5$, $-S(O)_yR^{10}$, $-SO_2OH$;

R^4 and R^5 are independently hydrogen, C_1-C_3 alkyl, C_3-C_7 cycloalkyl, $-C(O)R^9$, or R^4 and R^5, together with the nitrogen atom to which they are bound, form a heterocyclyl;

R^6 is alkylene, arylene, heteroarylene, C_3-C_7 cycloalkylene, alkenylene, C_3-C_7 cycloalkenylene, or alkynylene;

R^9 is C_1-C_6 alkyl or C_1-C_6 haloalkyl;

R^{10} is NH_2, C_1-C_6 alkyl, C_1-C_6 hydroxyalkyl, aryl, heteroaryl, or heterocyclyl; and

R^{11} is C_1-C_6 alkyl.

7. A compound as claimed in claim 1 or 2, wherein D is N.

8. A compound as claimed in claims 1 to 4 wherein R^1 is hydrogen or C_1-C_6 alkyl.

9. A compound as claimed in claim 1 to 4, wherein R^1 is hydrogen.

10. A compound as claimed in claim 1 to 4, wherein R^1 is C_1-C_6 alkyl.

11. A compound as claimed in claim 1 to 4, wherein R^2 is hydrogen, C_1-C_6 alkenyl, heterocyclyl, aryl, heteroaryl, $-OR^8$, $S(O)_yR^7$, and $-NR^4R^5$.

12. A compound as claimed in claim 1 to 4, wherein R^2 is hydrogen, heterocyclyl, aryl, heteroaryl, or $-OR^8$.

13. A compound as claimed in claim 1 to 4, wherein R^2 is hydrogen.

14. A compound as claimed in claim 1 to 4, wherein R^2 is $-OR^8$ where R^8 is hydrogen, methyl and isopropyl.

15. A compound as claimed in claim 1 to 4, wherein R^2 is heterocyclyl, aryl, or heteroaryl.

16. A compound as claimed in claim 1, wherein Q is $N(R^8)$, p is 1, and Q^1 is C_1-C_6 alkyl, C_3-C_7 cycloalkyl, C_1-C_6 haloalkyl,, or aryl.

17. A compound as claimed in claim 1, wherein Q is $N(R^8)$, p is 1, and Q^1 is C_3-C_7 cycloalkyl.

18. A compound as claimed in claim 1, wherein Q is $N(R^8)$, p is 1, and Q^1 is cyclopropyl.

19. A compound as claimed in claim 1, wherein wherein Q is $N(R^8)$, p is 1, and Q^1 is aryl.

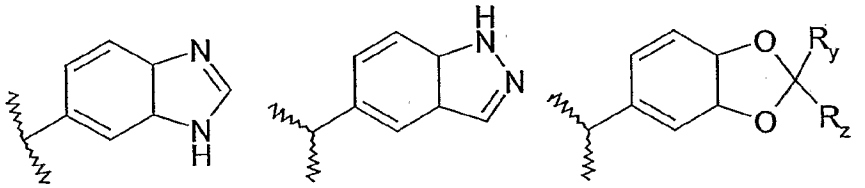
20. A compound as claimed in claim 1, wherein Q is $N(R^8)$, p is 1, and Q^1 is phenyl or phenyl substituted with at least one of C_1-C_6 alkyl, halo, cyano, carboxy, C_1-C_6 haloalkyl, C_1-C_6 alkoxy, nitro, heteroaryl, or heterocyclyl.

21. A compound as claimed in claims 4 to 6, wherein b is 1, 2, or 3 and R^x is hydrogen, halogen, C_1-C_6 alkyl, C_1-C_6 hydroxyalkyl, -CN, -C(O)OH, $-OC(O)R^{11}$, C_1-C_6 haloalkyl, $-NO_2$, -OH, $-OR^9$, aryl, heteroaryl, heterocyclyl, $-NR^4R^5$, $-R^6NR^4R^5$, $-C(O)N(H)R^6NR^4R^5$, $-S(O)_yR^{10}$, or $-SO_3H$.

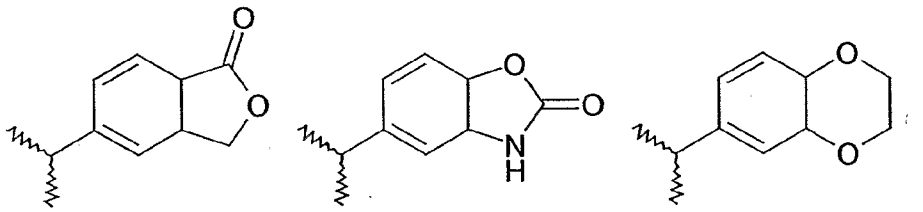
22. A compound as claimed in claims 4 to 6, wherein; b is 1 or 2 and R^x is halogen, C_1-C_6 alkyl, C_1-C_6 hydroxyalkyl, -CN, C_1-C_6 haloalkyl, $-NO_2$, heterocyclyl, or $-NR^4R^5$.

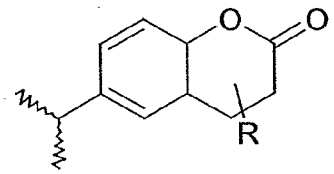
23. A compound as claimed in claims 4 to 6, wherein b is 1 and R^x is $-CH_3$, $-CH_2CH_3$, $-CF_3$, -CN, or $-NO_2$.

24. A compound as claimed in claims 4 to 5, wherein b is 2 and the two R^x groups together with the phenyl group to which they are bound form a fused group selected from:



wherein Ry and Rz are independently selected from hydrogen and halogen,





, wherein R is selected from –CF3, halogen, or hydrogen.

25. A compound as claimed in claim 6, wherein b is 1, 2, or 3; y is 0, 1, or 2; and R^x is independently selected from hydrogen, halogen, C_1-C_6 alkyl, C_1-C_6 hydroxyalkyl, -CN, -C(O)OH, $-OC(O)R^{11}$, C_1-C_6 haloalkyl, $-NO_2$, -OH, $-OR^9$, aryl, heteroaryl, heterocyclyl, $-NR^4R^5$, $-R^6NR^4R^5$, $-C(O)N(H)R^6NR^4R^5$, $-S(O)_yR^{10}$, or $-SO_3H$.

26. A compound as claimed in claim 6, wherein b is 1 or 2 and R^x is independently selected from hydrogen, halogen, C_1-C_6 alkyl, -CN, -C(O)OH, - C_1-C_6 haloalkyl, $-NO_2$, -OH, or $-OR^9$.

27. A compound as claimed in claim 6, wherein b is 1 or 2 and R^x is independently selected from hydrogen, halogen, -CN, - C_1-C_6 haloalkyl, or $-NO_2$.

28. A compound as claimed in claim 6, wherein b is 1 and R^x is selected from –F, $-CH_3$, -CN, $-CF_3$, or $-NO_2$.

29. A compound as claimed in claim 1, selected from the group consisting of:

N-cyclopropyl-4-pyrazolo[1,5-*b*]pyridazin-3-yl-2-pyrimidinamine;

N-cyclopropyl-*N*-methyl-4-pyrazolo[1,5-*b*]pyridazin-3-yl-2-pyrimidinamine;

4-pyrazolo[1,5-*b*]pyridazin-3-yl-*N*-(2,2,2-trifluoroethyl)-2-pyrimidinamine;

N-phenyl-4-pyrazolo[1,5-*b*]pyridazin-3-yl-2-pyrimidinamine;

N-(4-chlorophenyl)-4-pyrazolo[1,5-*b*]pyridazin-3-yl-2-pyrimidinamine;

N-(4-fluorophenyl)-4-pyrazolo[1,5-*b*]pyridazin-3-yl-2-pyrimidinamine;

3-[(4-pyrazolo[1,5-*b*]pyridazin-3-yl-2-pyrimidinyl)amino]benzonitrile;

4-[(4-pyrazolo[1,5-*b*]pyridazin-3-yl-2-pyrimidinyl)amino]benzoic acid;

4-pyrazolo[1,5-*b*]pyridazin-3-yl-*N*-[3-(trifluoromethyl)phenyl]-2-pyrimidinamine;

N-(3-nitrophenyl)-4-pyrazolo[1,5-*b*]pyridazin-3-yl-2-pyrimidinamine;

N-(2-chlorophenyl)-4-pyrazolo[1,5-*b*]pyridazin-3-yl-2-pyrimidinamine;

N-(4-methoxyphenyl)-4-pyrazolo[1,5-*b*]pyridazin-3-yl-2-pyrimidinamine;

4-pyrazolo[1,5-*b*]pyridazin-3-yl-*N*-(3,4,5-trimethoxyphenyl)-2-pyrimidinamine;

N-[3-(1,3-oxazol-5-yl)phenyl]-4-pyrazolo[1,5-*b*]pyridazin-3-yl-2-pyrimidinamine;

N-(4-pyrazolo[1,5-*b*]pyridazin-3-yl-2-pyrimidinyl)-1*H*-benzimidazol-6-amine;

N-(4-pyrazolo[1,5-*b*]pyridazin-3-yl-2-pyrimidinyl)-1,3-benzoxazol-2-amine;

N-(6-chloro-1*H*-benzimidazol-2-yl)-*N*-(4-pyrazolo[1,5-*b*]pyridazin-3-yl-2-pyrimidinyl)amine;

N-(4-chlorobenzyl)-4-pyrazolo[1,5-*b*]pyridazin-3-yl-2-pyrimidinamine;

N^1,N^1-dimethyl-N^3-(4-pyrazolo[1,5-*b*]pyridazin-3-yl-2-pyrimidinyl)-1,3-propanediamine methanesulfonate;

N-[3-(4-morpholinyl)propyl]-4-pyrazolo[1,5-*b*]pyridazin-3-yl-2-pyrimidinamine;

N-[3-(4-methyl-1-piperazinyl)propyl]-4-pyrazolo[1,5-*b*]pyridazin-3-yl-2-pyrimidinamine;

1-{3-[(4-pyrazolo[1,5-*b*]pyridazin-3-yl-2-pyrimidinyl)amino]propyl}-2-pyrrolidinone;

N-[3-chloro-4-(4-methyl-1-piperazinyl)phenyl]-4-pyrazolo[1,5-*b*]pyridazin-3-yl-2-pyrimidinamine;

N-[4-(4-methyl-1-piperazinyl)phenyl]-4-pyrazolo[1,5-*b*]pyridazin-3-yl-2-pyrimidinamine;

N-[3-methyl-4-(4-methyl-1-piperazinyl)phenyl]-4-pyrazolo[1,5-*b*]pyridazin-3-yl-2-pyrimidinamine;

N-[4-(4-methyl-1-piperazinyl)-3-(trifluoromethyl)phenyl]-4-pyrazolo[1,5-*b*]pyridazin-3-yl-2-pyrimidinamine;

N-[3-chloro-4-(4-morpholinyl)phenyl]-4-pyrazolo[1,5-*b*]pyridazin-3-yl-2-pyrimidinamine;

N-{4-[(diethylamino)methyl]phenyl}-4-pyrazolo[1,5-*b*]pyridazin-3-yl-2-pyrimidinamine;

N-[2-(diethylamino)ethyl]-4-[(4-pyrazolo[1,5-*b*]pyridazin-3-yl-2-pyrimidinyl)amino]benzamide;
N-cyclopropyl-4-(2-methylpyrazolo[1,5-*b*]pyridazin-3-yl)-2-pyrimidinamine;

N-cyclopropyl-4-(2-ethylpyrazolo[1,5-*b*]pyridazin-3-yl)-2-pyrimidinamine;

4-(2-butylpyrazolo[1,5-*b*]pyridazin-3-yl)-*N*-cyclopropyl-2-pyrimidinamine;

N-[4-(4-methyl-1-piperazinyl)phenyl]-4-(2-methylpyrazolo[1,5-*b*]pyridazin-3-yl)-2-pyrimidinamine;

4-(2-ethylpyrazolo[1,5-*b*]pyridazin-3-yl)-*N*-[4-(4-methyl-1-piperazinyl)phenyl]-2-pyrimidinamine;

4-(2-butylpyrazolo[1,5-*b*]pyridazin-3-yl)-*N*-[4-(4-methyl-1-piperazinyl)phenyl]-2-pyrimidinamine;

N-cyclopropyl-4-(6-methoxypyrazolo[1,5-*b*]pyridazin-3-yl)-2-pyrimidinamine;

4-(6-methoxypyrazolo[1,5-*b*]pyridazin-3-yl)-*N*-[4-(4-methyl-1-piperazinyl)phenyl]-2-pyrimidinamine;

3-[2-(cyclopropylamino)-4-pyrimidinyl]pyrazolo[1,5-*b*]pyridazin-6-ol;

N-cyclopropyl-4-(6-isopropoxypyrazolo[1,5-*b*]pyridazin-3-yl)-2-pyrimidinamine;

N-[4-(6-isopropoxypyrazolo[1,5-*b*]pyridazin-3-yl)-2-pyrimidinyl]-*N*-[4-(4-methyl-1-piperazinyl)phenyl]amine;

3-[2-(cyclopropylamino)-4-pyrimidinyl]pyrazolo[1,5-*b*]pyridazin-6-yl trifluoromethanesulfonate;

4-[6-(2-chlorophenyl)pyrazolo[1,5-*b*]pyridazin-3-yl]-*N*-cyclopropyl-2-pyrimidinamine;

N-cyclopropyl-4-[6-(2-thienyl)pyrazolo[1,5-*b*]pyridazin-3-yl]-2-pyrimidinamine;

N-cyclopropyl-4-[6-(4-fluorophenyl)pyrazolo[1,5-*b*]pyridazin-3-yl]-2-pyrimidinamine;

N-cyclopropyl-4-(6-vinylpyrazolo[1,5-*b*]pyridazin-3-yl)-2-pyrimidinamine;

N-cyclopropyl-4-[6-(4-morpholinyl)pyrazolo[1,5-*b*]pyridazin-3-yl]-2-pyrimidinamine;

N-cyclopentyl-3-[2-(cyclopropylamino)-4-pyrimidinyl]pyrazolo[1,5-*b*]pyridazin-6-amine;

N-cyclopropyl-4-[6-(1-pyrrolidinyl)pyrazolo[1,5-*b*]pyridazin-3-yl]-2-pyrimidinamine;

N-cyclopropyl-4-[6-(2-fluoro-4-pyridinyl)pyrazolo[1,5-*b*]pyridazin-3-yl]-2-pyrimidinamine;

N-cyclopropyl-4-[6-(phenylsulfanyl)pyrazolo[1,5-*b*]pyridazin-3-yl]-2-pyrimidinamine;

4-[6-(4-fluorophenyl)pyrazolo[1,5-*b*]pyridazin-3-yl]-*N*-(4-methoxyphenyl)-2-pyrimidinamine;

4-[6-(4-fluorophenyl)pyrazolo[1,5-*b*]pyridazin-3-yl]-*N*-[4-(4-methyl-1-piperazinyl)phenyl]-2-pyrimidinamine;

N^1,N^1-dimethyl-N^4-{4-[6-(4-morpholinyl)pyrazolo[1,5-*b*]pyridazin-3-yl]-2-pyrimidinyl}-1,4-benzenediamine;

1-(dimethylamino)-3-[4-({4-[6-(4-morpholinyl)pyrazolo[1,5-*b*]pyridazin-3-yl]-2-pyrimidinyl}amino)phenoxy]-2-propanol;

N-(1,3-benzodioxol-5-yl)-4-pyrazolo[1,5-*b*]pyridazin-3-yl-2-pyrimidinamine;

N-(2,3-dihydro-1,4-benzodioxin-6-yl)-4-pyrazolo[1,5-*b*]pyridazin-3-yl-2-pyrimidinamine;

N-[3-methoxy-5-(trifluoromethyl)phenyl]-4-pyrazolo[1,5-*b*]pyridazin-3-yl-2-pyrimidinamine;

4-[(4-pyrazolo[1,5-*b*]pyridazin-3-yl-2-pyrimidinyl)amino]benzonitrile;

N-(4-nitrophenyl)-4-pyrazolo[1,5-*b*]pyridazin-3-yl-2-pyrimidinamine;

N-(3-methoxyphenyl)-4-pyrazolo[1,5-*b*]pyridazin-3-yl-2-pyrimidinamine;

N-(3,5-dimethylphenyl)-4-pyrazolo[1,5-*b*]pyridazin-3-yl-2-pyrimidinamine;

N-(4-aminosulfonylphenyl)-4-pyrazolo[1,5-b]pyridazin-3-yl-2-pyrimidinamine; and

N-(4-methylsulfonylphenyl)-4-pyrazolo[1,5-b]pyridazin-3-yl-2-pyrimidinamine; or

a salt, solvate, or physiologically functional derivative thereof.

30. A pharmaceutical composition, comprising: a therapeutically effective amount of a compound as claimed in any one of claims 1 to 29, or a salt, solvate, or a physiologically functional derivative thereof and one or more of pharmaceutically acceptable carriers, diluents and excipients.

31. The pharmaceutical composition of claim 30, further comprising at least one anti-neoplastic agent.

32. A pharmaceutical composition, comprising: a therapeutically effective amount of a compound as claimed in claims 1 to 29, or a salt, solvate, or a physiologically functional derivative thereof and one or more of pharmaceutically acceptable carriers, diluents and excipients for preventing or reducing the severity of epithelial cytotoxicity in a subject receiving cytotoxic therapy.

33. A method of treating a disorder in a mammal, said disorder being mediated by inappropriate CDK activity, comprising: administering to said mammal a therapeutically effective amount of a compound as claimed in any one of claims 1 to 29, or a salt, solvate, or a physiologically functional derivative thereof.

34. The method of claim 33, wherein the disorder is cancer.

35. The method of claim 33, wherein the CDK activity is CDK2 activity.

36. The method of claim 33, wherein the CDK activity is CDK4 activity.

37. A compound as claimed in any of claims 1 to 29, or a salt, solvate, or a physiologically functional derivative thereof for use in therapy.

38. Use of a compound as claimed in any of claims 1 to 29, or a salt, solvate, or a physiologically functional derivative thereof in the preparation of a medicament for use in the treatment of a disorder mediated by inappropriate CDK activity.

39. The use of claim 38, wherein the disorder is cancer.

40. The use of claim 38, wherein the CDK activity is CDK2 activity.

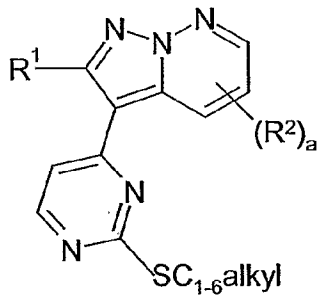
41. The use of claim 38, wherein the CDK activity is CDK4 activity.

42. A method of preventing or reducing the severity of epithelial cytotoxicity in a patient receiving cytotoxic therapy, comprising administering to said patient a therapeutically effective amount of a compound as claimed in any of claims 1 to 29 or a salt, solvate, or physiologically functional derivative thereof.

43. A method of treating cancer in a mammal, including administering to said mammal a therapeutically effective amount of a compound as claimed in any of claims 1 to 29, or salt, solvate or physiologically functional derivative thereof.

44. A method of treating cancer in a mammal, including administering to said mammal therapeutically effective amounts of (i) a compound as claimed in any of claims 1 to 29, or salt, solvate or physiologically functional derivative thereof and (ii) at least one additional anti-cancer therapy.

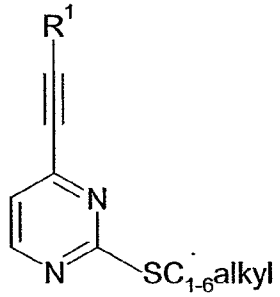
45. A process for preparing a compound of formula (Q)



(Q)

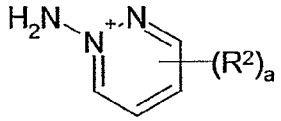
comprising, the step of:

(i) reacting in the presence of a base a compound of formula (U)



(U)

with a compound of formula (E)



(E)

wherein

R^1 is hydrogen, C_1-C_6 alkyl, C_1-C_4 alkenyl, C_1-C_4 alkynyl, C_1-C_3 alkoxy, halogen, hydroxy, cyano, $-S(O)_yC_1$-C_3 alkyl, $-NR^4R^5$;

a is 1 or 2; and

R^2 is hydrogen, C_1-C_6 alkyl, C_1-C_6 alkenyl, C_1-C_6 alkynyl, C_1-C_6 haloalkyl, C_3-C_7 cycloalkyl, halogen, heterocyclyl, aryl, heteroaryl, cyano, azido, nitro, $-OR^8$, $-OR^6R^8$, $-R^6R^7$, $-R^6R''$,

$S(O)_yR^7$, $-C(O)R^7$, $-C(O)OR^7$, $-C(O)NR^4R^5$, $-NR'(C=NR^4)NR^4R^5$, $-OC(O)NR^4R^5$, $-OC(O)OR^7$, $-C(=NR^4)NR^4R^5$, $-NR^4R^5$, $-OC(O)R^7$, $-NR^7C(O)R^7$.

46. A process as claimed in claim 45, wherein the base is an amine.

47. A process as claimed in claim 45, wherein the base is an alkali metal hydroxide.

48. A method of treating a disorder in a mammal, said disorder being mediated by inappropriate CDK4 activity, comprising: administering to said mammal therapeutically effective amounts of (i) a compound as claimed in any one of claims 1 to 29, or a salt, solvate or physiologically functional derivative thereof and (ii) an agent to inhibit growth factor receptor function.

49. The method of claim 48, wherein the agent to inhibit growth factor receptor function inhibits the function of platelet derived growth factor receptor.

50. The method of claim 48, wherein the agent to inhibit growth factor receptor function inhibits the function of epidermal growth factor receptor.

51. The method of claim 48, wherein the agent to inhibit growth factor receptor function inhibits the function of the erbB2 receptor.

52. The method of claim 48, wherein the agent to inhibit growth factor receptor function inhibits the function of the VEGF receptor.

53. The method of claim 48, wherein the agent to inhibit growth factor receptor function inhibits the function of the Tie-2 receptor.

54. The method of claim 48, wherein the agent to inhibit growth factor receptor function inhibits the function of the epidermal growth factor receptor and erbB2.

55. The method of claim 48, wherein the agent to inhibit growth factor receptor function inhibits the function of the VEGF receptor and the TIE-2 receptor.

56. The method of claim 48, wherein the disorder is cancer.